Vision and Traumatic Brain Injury: The Outlook for Therapeutics
Saturday, April 30, 2016. 10am – 1pm PDT, Washington State Convention Center, Seattle

Researchers are learning about the significance of visual function in the evaluation of traumatic brain injury (TBI). During this interactive session, vision scientists and neuropathologists will discuss the impact of systematic, early assessment of the visual system on the potential for therapeutic protection and intervention against TBI. The program provides opportunities for interactions between attendees, panelists and patients. Opening and summary remarks to be provided by Congressman Jim McDermott and NFL Hall of Fame Honoree Jim Zorn, respectively.

Preliminary Program
Introduction:
John I. Clark, PhD, FARVO

Congressman Jim McDermott, MD, WA-7

Part 1: Traumatic brain injury and visual function
Co-moderators:
Mary G. Lawrence, MD, MPH
DoD/VA Vision Center of Excellence. University of Minnesota Medical School

Donald A. Gagliano, MD, MHA
Global Medical Innovation, San Antonio

Panel
CTE: A Late Effect of Football and Military Trauma
Ann C. McKee, MD, Chief of Neuropathology, National Veterans Affairs and ALS Brain Bank. Center for the Study of Traumatic Encephalopathy. Boston University, School of Medicine

Veterans and contact sports athletes who experience concussions and other brain trauma are at risk for long-term neurologic and behavioral problems, including chronic traumatic encephalopathy (CTE). CTE has been associated with American football, boxing, soccer, ice hockey, baseball, rugby and military-related activities. Veterans are particularly susceptible to CTE given their combined exposure to traumatic brain injuries from sports, recreational activities, combat exposure, motor vehicle accidents and other trauma. There is also increasing evidence that sub-concussive hits, smaller impacts that are not severe enough to cause concussion symptoms, are associated with CTE. In our brain bank series, 16% of individuals diagnosed with CTE had no history of concussion suggesting that sub-concussive hits and cumulative exposure to trauma are sufficient to lead to CTE.

The clinical symptoms of CTE typically develop insidiously, years to decades after exposure to repetitive brain trauma and progress slowly over years. Early behavioral symptoms include explosivity, verbal and physical violence, loss of control, impulsivity, paranoia and rage behaviors. Cognitively, the most prominent deficits are memory, executive functioning, impaired attention and cognitive loss. Approximately 60% of subjects with CTE develop visual symptoms including blurred vision, double vision, vision loss or light sensitivity. Currently, there is no way to diagnose CTE during life; if specific changes can be identified in the eye in CTE, they might be useful for diagnosing CTE before death. The incidence and prevalence of CTE is not known, however, several recent studies suggest that CTE is more common than currently appreciated.

Challenges on and off the Battlefield
Master Sergeant Eric Marts (Retired Army)
Master Sergeant Marts will share the challenges he’s faced – from both TBI and the Department of Veterans Affairs – following his deployment to Iraq in 2005 – 2007.

Experimental Approach to Neurotrauma and the Eye
Lee E. Goldstein, MD, PhD, Neurology, Pathology, Ophthalmology, and Bioengineering, Boston University, School of Medicine

TBI is a leading cause of death, disability, and visual impairment around the world. Contact sports and military-related head injuries are also associated with a wide range of persistent symptoms, including vision disability and blindness, migraine-like headache and other facial pain disorders, mood and behavioral changes, and cognitive problems. TBI is also associated with increased risk of later development of neurodegenerative disease, including Alzheimer’s disease (AD) and chronic traumatic encephalopathy (CTE). The mechanisms and pathways that link TBI, persistent neurobehavioral problems, and neurodegenerative diseases are poorly understood. This presentation will focus on new experimental animal models of TBI that replicate injury biomechanics, pathological consequences, and chronic neurobehavioral impairments associated with military- and sports-related TBI in humans. We have developed, validated, and compared new animal models of blast and impact neurotrauma that accurately reproduce core clinical features of TBI and CTE in humans. Analysis of experimental results in these animal models have uncovered key determinants and mechanisms that trigger acute and chronic effects of neurotrauma in humans. The availability of these animal models opens new avenues for development of urgently-needed diagnostics, treatments, and rehabilitative strategies for people affected by TBI and its aftermath. Implications for trauma-related ocular injury, visual disability, and blindness will be discussed.

Do Visual Manifestations of TBI Progress?
Randy H. Kardon, MD, PhD, Director, VA Center of Excellence for Prevention and Treatment of Visual Loss, Pomerantz Chair in Ophthalmology, Carver College of Medicine, University of Iowa

Very little is known about the chronic visual consequences of mild TBI, its progression, and its correlation with central nervous system (CNS) deficits. Currently, it is not known if neuronal loss in the retina and brain after mild TBI continues to progress over time, giving rise to Chronic Traumatic Encephalopathy (CTE). Closing this knowledge gap will be important for understanding and treating TBI-related visual symptoms and for establishing whether ocular biomarkers can be used to predict risk of CNS dysfunction and its progression over time. A more complete picture of the spectrum of visual sensory disturbances after mild TBI will be obtained by utilizing more detailed tests of visual function and ocular motility, as well as newer structural analyses of the retina, combined with functional MRI imaging of visual pathways in the brain.

Break

Part 2: Potential therapies based on disturbances in vision
Co-moderators:
Tonia Rex, PhD, Department of Ophthalmology and Visual Sciences, Vanderbilt University
Donald A. Gagliano, MD, MHA
Global Medical Innovation, San Antonio

Panel
Potential Therapies Based on Disturbance in Vision
Wing Commander Robert AH Scott, MBBS, FRCS(Ed), FRCOphth, DMI; University of Birmingham, United Kingdom
A patient exposed to an explosive blast wave may have limited clinical evidence of injury, but significant occult damage at the microscopic level. The spectrum of injury after an ocular primary blast injury (PBI) can be divided anatomically into anterior and posterior segment injuries, with the posterior segment of the eye particularly susceptible. In the anterior segment, the conjunctiva is frequently affected with lacerations and subconjunctival haemorrhages. The iris and ciliary body can be damaged with hyphaema, traumatic iritis with iris sphincter rupture, dialysis and spiral tears. In common with blunt force trauma, damage to the delicate angle structures can cause angle recession with secondary glaucoma, cyclodialysis clefts, or iridodialysis. Ciliary muscle atrophy may result in reduced accommodation making reading difficult, with associated eyestrain. Traumatic cataracts are commonly seen after PBI, but may spontaneously resolve.

The posterior segment is affected in around 60% of cases, even though the blast wave traverses the anterior segment to reach it. Injuries can include posterior vitreous detachments, with or without associated vitreous hemorrhage, retinal tears and detachments, as well as macula commotion retinæ. Traumatic optic neuropathy is a well-known effect of PBI and optic atrophy often follows massive retinal atrophy, induced vasoconstriction of the optic nerve blood supply, or mechanical disruption of optic nerve axons as they exit the posterior globe through the lamina cribrosa. This presentation outlines potential new treatments for some of these blinding injuries using small interfering RNA molecules and inhibitors of apoptosis. Further new treatments of traumatic glaucoma corneal and intraocular scarring using the matrikine Decorin will be discussed.

*Blast Concussion and Mild TBI in Veterans: Implications for Vision*

**Elaine R. Peskind, MD, Department of Psychiatry and Behavioral Sciences; Veterans Affairs Puget Sound Health Care System, University of Washington**

Repetitive blast concussion mild TBI has been termed the “signature injury” of the wars in Iraq and Afghanistan. Repetitive mild TBI may place young service members and veterans at risk for long-term brain degeneration. We study blast concussion mild TBI in both veterans and in a mouse model that mimics battlefield-relevant blast concussion. In both veterans and mice, we have found that blast concussion produces abnormalities in the cerebellum, the part of the brain that integrates sensation and movement. These abnormalities may have implications for visual abnormalities following blast concussion.

*The Link between Photophobia and Head Injury*

**Andrew T. Hartwick, OD, PhD, College of Optometry, The Ohio State University**

We have been working with patients that have had previous head injuries and have experienced increased light sensitivity (photophobia) since the injury. We have been examining the response of their pupils to flashes of red and blue light, in addition to quantifying their sleep habits and light exposure during their daily lives. Even though photophobia is commonly associated with traumatic brain injury, we still don’t know exactly why. Many of the subjects we recruited for our study had great vision (20/20 acuity) and what appeared to be healthy eyes, as assessed using standard eye examination techniques. Yet, the chronic photophobia they experienced often significantly impacted their life and altered their daily activities. It is my hope that we will soon not only understand why photophobia is linked to head trauma, but use this information to develop better treatments for this debilitating symptom.

**Summary Remarks:**

Jim Zorn, NFL Hall of Fame Honoree